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Applicants: Alizon et al.

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### Search Strategy

FILE 'USPATFULL' ENTERED AT 19:20:53 ON 22 APR 1998

L1 E ALIZON MARC/IN  
11 S E3  
E MONTAGNIER LUC/IN  
L2 42 S E3  
L3 32 S L2 NOT L1  
L4 24 S L3 AND LAV  
E LUCIW PAUL  
E LUCIW, PAUL/IN  
E LUCIW PAUL/IN  
L5 4 S E3 OR E4  
E LEVY JAY/IN  
L6 8 S E4

FILE 'MEDLINE' ENTERED AT 19:39:54 ON 22 APR 1998

E ALIZON, M/AU  
L7 35 S E2  
L8 5 S L7 AND LAV  
L9 30 S L7 NOT L8  
E MONTAGNIER LUC/AU  
L10 274 S E2  
L11 27 S L10 AND LAV  
L12 1 S LAVMAL  
L13 1 S LAV AND MAL  
E HAHN B/AU  
L14 161 S E6  
L15 8 S L14 AND PY=1985  
L16 3 S L14 AND PY=1986  
E RATNER LEE/AU  
E RATNER L/AU  
L17 125 S E3  
E GALLO R C/AU

L1 ANSWER 10 OF 11 USPATFULL  
91:59054 Variant of LAV viruses.

\*\*\*Alizon, Marc\*\*\* , Paris, France  
Sonigo, Pierre, Paris, France  
Wain-Hobson, Simon, Montigny les Bretonneux, France  
Montagnier, Luc, Le Plessis Robinson, France  
Institut Pasteur, Paris, France (non-U.S. corporation)  
US 5034511 910723  
APPLICATION: US 87-38332 870413 (7)  
DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A variant of a LAV virus, designated LAV.sub.ELI and capable of causing AIDS. The cDNA and antigens of the LAV.sub.ELI virus can be used for the diagnosis of AIDS and pre-AIDS.

CLM What is claimed is:  
1. An isolated or synthetic peptide comprising an amino acid sequence that is a fragment of the following amino acid sequence: ##STR1## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine, and wherein said fragment comprises at least one amino acid sequence selected from the group consisting of amino-acyl residues 37-130, amino-acyl residues 211-289, amino-acyl residues 488-530, amino-acyl residues 490-620, amino-acyl residues 680-700, amino-acyl residues 1-530, amino-acyl residues 34-530, amino-acyl residues 531-877 of an envelope glycoprotein of LAV.sub.ELI virus.

2. An isolated or synthetic peptide as claimed in claim 1, wherein said amino acid sequence comprises a sequence selected from the group consisting of amino-acyl residues 37 to 130, 211 to 289, and 488 to 530.

3. An isolated or synthetic peptide as claimed in claim 1, wherein said amino acid sequence comprises amino-acyl residues 490 to 620 or 680 to 700.

4. An isolated or synthetic peptide as claimed in claim 1, wherein said amino acid sequence comprises a sequence selected from the group consisting of: amino-acyl residues 1 to 530; amino-acyl residues 34 to 530; and amino-acyl residues 531 to 877.

5. An immunogenic composition comprising an isolated or synthetic peptide as claimed in claim 1, and a physiologically acceptable carrier.

6. A diagnostic kit for the in vitro detection of antibodies against a lymphadenopathy associated virus comprising an isolated or synthetic peptide as claimed in claim 1, and a reagent for detecting the formation of peptide/antibody complex.

7. An isolated or synthetic peptide comprising an amino acid sequence that is a fragment of the following amino acid sequence: ##STR2## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine, and wherein said fragment comprises a p25 peptide comprising amino-acyl residues 138-385 of gag protein of LAV.sub.ELI virus.

8. An isolated or synthetic peptide comprising an amino acid sequence that is a fragment of the following amino acid sequence: ##STR3## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine, and wherein said fragment comprises a p13 peptide comprising amino-acyl residues 385-519 of gag protein of LAV.sub.ELI virus.

9. An isolated or synthetic peptide comprising an amino acid sequence: ##STR4## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine.

L1 ANSWER 11 OF 11 USPATFULL

91:54851 Variant of LAV viruses.

\*\*\*Alizon, Marc\*\*\* , Paris, France

Sonigo, Pierre, Paris, France

Wain-Hobson, Simon, Montigny Les Bretonneux, France

Montagnier, Luc, Le Plessis Robinson, France

Institut Pasteur, Paris, France (non-U.S. corporation)

US 5030714 910709

APPLICATION: US 87-38330 870413 (7)

PRIORITY: EP 86-401380 860623

DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- AB A variant of the LAV virus, designated LAV.sub.MAL and capable of causing AIDS. The cDNA and antigens of the LAV.sub.MAL virus can be used for the diagnosis of AIDS and pre-AIDS.
- CLM What is claimed is:
1. An isolated or synthetic peptide comprising an amino acid sequence that is a fragment of the following amino acid sequence: ##STR1## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine, and wherein said fragment comprises at least one amino acid sequence selected from the group consisting of amino-acyl residue 37-130, amino-acyl residues 211-289, amino-acyl residues 488-530, amino-acyl residues 490-620, amino-acyl residues 680-700, amino-acyl residues 1-530, amino-acyl residues 34-530, amino-acyl residues 531-877 of an envelope glycoprotein of LAV.sub.MAL virus.
  2. An immunogenic composition comprising an isolated or synthetic peptide as claimed in claim 1 and a physiologically acceptable carrier, wherein said immunogenic composition is capable of eliciting an immune response to said peptide in a host.
  3. An immunogenic composition as claimed in claim 2, wherein said peptide is coupled to a physiologically acceptable and non-toxic carrier molecule that is capable of enhancing the immunogenicity of the peptide.
  4. An immunogenic composition as claimed in claim 3, wherein said carrier molecule is a natural protein or a synthetic macromolecular carrier.
  5. An immunogenic composition as claimed in claim 4, wherein said natural protein is selected from the group consisting of tetanus toxoid, ovalbumin, serum albumin, and hemocyanin.
  6. An immunogenic composition as claimed in claim 4, wherein said synthetic macromolecular carrier is polylysine or poly(D-L alanine)-poly(L-lysine).
  7. The peptide of claim 1, wherein said peptide is a glycoprotein.
  8. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 37-130 of the envelope glycoprotein of LAV.sub.MAL virus.
  9. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 211-289 of the envelope glycoprotein of LAV.sub.MAL virus.
  10. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 488-530 of the envelope glycoprotein of LAV.sub.MAL virus.
  11. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 490-620 of the envelope glycoprotein of LAV.sub.MAL virus.
  12. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 680-700 of the envelope glycoprotein of LAV.sub.MAL virus.
  13. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 1-530 of the envelope glycoprotein of LAV.sub.MAL virus.

14. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 34-530 of the envelope glycoprotein of LAV.sub.MAL virus.

15. An isolated or synthetic peptide as claimed in claim 1, wherein said fragment comprises amino-acyl residues 531-877 of the envelope glycoprotein of LAV.sub.MAL virus.

16. An isolated or synthetic peptide comprising an amino acid sequence that is a fragment of the following amino acid sequence: ##STR2## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine, and wherein said fragment comprises a p25 peptide comprising amino-acyl residues 138-385 of gag protein of LAV.sub.MAL virus.

17. An immunogenic composition comprising an isolated or synthetic peptide as claimed in claim 16 and a physiologically acceptable carrier, wherein immunogenic composition is capable of eliciting an immune response to said peptide in a host.

18. An isolated or synthetic peptide comprising an amino acid sequence that is a fragment of the following amino acid sequence: ##STR3## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine, and wherein said fragment comprises a p13 peptide comprising amino-acyl residues 385-519 of gag protein of LAV.sub.MAL virus.

19. An immunogenic composition comprising an isolated or synthetic peptide as claimed in claim 18 and a physiologically acceptable carrier, wherein immunogenic composition is capable of eliciting an immune response to said peptide in a host.

20. An isolated or synthetic peptide comprising an amino acid sequence: ##STR4## wherein, in said amino acid sequence, A is alanine, C is cysteine, D is aspartic acid, E is glutamic acid, F is phenylalanine, G is glycine, H is histidine, I is isoleucine, K is lysine, L is leucine, M is methionine, N is asparagine, P is proline, Q is glutamine, R is arginine, S is serine, T is threonine, V is valine, W is tryptophan, and Y is tyrosine.

L4 ANSWER 1 OF 24 USPATFULL

97:106928 Nucleotide sequences derived from the genome of retroviruses of the HIV-1, HIV-2 and SIV type, and their uses in particular for the amplification of the genomes of these retroviruses and for the in vitro diagnosis of the disease due to these viruses.

Moncany, Maurice, Paris, France

\*\*\*Montagnier, Luc\*\*\*, Le Plessis-Robinson, France

Institut Pasteur, France (non-U.S. corporation) Institut National de la Sante et de la Recherche Medicale, France (non-U.S. corporation)

US 5688637 971118

APPLICATION: US 93-160465 931202 (8)

PRIORITY: FR 89-7354 890602

FR 89-12371 890920

DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to nucleotidic sequences derived from genomes of the HIV-1 type virus, or from genomes of the HIV-2 type virus, or of the SIV type virus, and their applications, especially as oligo-nucleotidic initiators of implementation of an

\$i (in vitro) method for the diagnosis of the infection of an individual by a virus of the HIV-1 and/or HIV-2 type.

CLM What is claimed is:

1. An oligonucleotide primer, said primer having a nucleotide sequence selected from the following group of nucleotides oriented in the 5'-3' direction: nucleotides 636-653, 854-872, 1369-1388, and 2021-2039 of the gag gene of HIV-1 Bru; nucleotides 900-881, 1385-1369, 1388-1369, and 2039-2021 of a nucleic acid sequence complementary to the gag gene of HIV-1 Bru; nucleotides 635-652, 864-888, 1403-1421, and 2055-2073 of the gag gene of HIV-1 Mal; nucleotides 916-897, 1419-1403, 1421-1403, and 2073-2055 of a nucleic acid sequence complementary to the gag gene of HIV-1 Mal; nucleotides 636-653, 848-872, 1369-1388, and 2024-2042 of the gag gene of HIV-1 Eli; nucleotides 900-881, 1385-1369, 1388-1369, and 2042-2024 of a nucleic acid sequence complementary to the gag gene of HIV-1 Eli; nucleotides 859-876, 1160-1184, 1687-1706, and 2329-2349 of the gag gene of HIV-2 ROD; nucleotides 1212-1193, 1703-1687, 1706-1687, and 2349-2329 of a nucleic acid sequence complementary to the gag gene of HIV-2 ROD; nucleotides 834-851, 1124-1148, 1651-1670, and 2299-2318 of the gag gene of SIV-MAC; and nucleotides 1176-1157, 1667-1651, 1670-1651, and 2318-2299 of a nucleic acid sequence complementary to the gag gene of SIV-MAC; nucleotides 5590-5610 of the vpr gene of HIV-1 Bru; nucleotides 5870-5849 of a nucleic acid sequence complementary to the vpr gene of HIV-1 Bru; nucleotides 5585-5605 of the vpr gene of HIV-1 Mal; nucleotides 5865-5844 of a nucleic acid sequence complementary to the vpr gene of HIV-1 Mal; nucleotides 5554-5574 of the vpr gene of HIV-1 Eli; nucleotides 5834-5813 of a nucleic acid sequence complementary to the vpr gene of HIV-1 Eli; nucleotides 6233-6296 of the vpr gene of HIV-2 ROD; nucleotides 6551-6531 of a nucleic acid sequence complementary to the vpr gene of HIV-2 ROD; nucleotides 6147-6170 of the vpr gene of SIV-MAC; and nucleotides 6454-6431 of a nucleic acid sequence complementary to the vpr gene of SIV-MAC; nucleotides 2620-2643, 3339-3361, 4186-4207, and 4992-5011 of the pol gene of HIV-1 Bru; nucleotides 2643-2620, 3361-3339, 4207-4186, and 5011-4992 of a nucleic acid sequence complementary to the pol gene of HIV-1 Bru; nucleotides 2615-2638, 3333-3356, 4181-4202, and 4987-5006 of the pol gene of HIV-1 Mal; nucleotides 2638-2615, 3356-3334, 4202-4181, and 5006-4987 of a nucleic acid sequence complementary to the pol gene of HIV-1 Mal; nucleotides 2584-2607, 3303-3325, 4150-4171, and 4956-4975 of the pol gene of HIV-1 Eli; nucleotides 2607-2584, 3325-3303, 4171-4150, and 4975-4956 of a nucleic acid sequence complementary to the pol gene of HIV-1 Eli; nucleotides 2971-2994, 3690-3712, 4534-4555, and 5340-5359 of the pol gene of HIV-2 ROD; nucleotides 2994-2971, 3712-3690, 4555-4534, and 5359-5340 of a nucleic acid sequence complementary to the pol gene of HIV-2 ROD; nucleotides 2887-3010, 3606-3628, 4450-4471, and 5275-5256 of a nucleic acid sequence complementary to the pol gene of SIV-MAC; 5256-5275 of the pol gene of SIV-MAC; and nucleotides 3010-2887, 3628-3606, 4471-4450, and nucleotides 9165-9185 and 9542-9564 of the nef2 gene of HIV-2 ROD; 9564-9542 and 9956-9933 of a nucleic acid sequence complementary to the nef2 gene of HIV-2 ROD; nucleotides 9139-9159 and 9516-9538 of the nef2 gene of SIV-MAC; 9538-9516 and 9839-9870 of a nucleic acid sequence complementary to the nef2 gene of SIV-MAC; nucleotides 5424-5450 and 5754-5775 of the vif2 gene of HIV-2 ROD; nucleotides 5775-5754 and 6082-6061 of a nucleic acid sequence complementary to the vif2 gene of HIV-2 ROD; nucleotides 5340-5366 and 5670-5691 of the vif2 gene of HIV-2 ROD; nucleotides 5691-5670 and 5995-5974 of a nucleic acid sequence complementary to the vif2 gene of SIV-MAC; nucleotides 5900-5918 of the vpx gene of HIV-2 ROD; nucleotides 6228-6208 of a nucleic acid sequence complementary to the vpx gene of HIV-2 ROD; nucleotides 5813-5831 of the vpx gene of HIV-2 ROD; nucleotides 6141-6121 of a nucleic acid sequence complementary to the vpx gene of SIV-MAC; nucleotides 6905-6930, 7055-7077, 7360-7384, 7832-7857, 8844-8869, 7629-7647, and 8224-8242 of the env gene of

HIV-1 Bru; nucleotides 6930-6905, 7384-7360, 7857-7832, 8869-8844, and 8242-8224 of a nucleic acid sequence complementary to the env gene of HIV-1 Bru; nucleotides 6903-6928, 7053-7075, 7821-7846, 7821-7846, 7612-7630, 8213-8231, and 8836-8861 of the env gene of HIV-1 Mal; nucleotides 6928-6903, 7373-7349, 7846-7821, 8861-8836, and 8231-8213 of a nucleic acid sequence complementary to the env gene of HIV-1 Mal; nucleotides 6860-6885, 7010-7032, 7306-7330, 7775-7800, 8787-8812, 7572-7590, and 8167-8185 of the env gene of HIV-1 Eli; and nucleotides 6885-6860, 7330-7306, 7800-7775, 8812-8787, and 8185-8167 of a nucleic acid sequence complementary to the env gene of HIV-1 Eli; nucleotides 9116-9136 of the nef1 gene of HIV-1 Bru; nucleotides 9136-9116 and 9503-9483 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Bru; nucleotides 9117-9137 of the nef1 gene of HIV-1 Mal; and nucleotides 9137-9117 and 9505-9484 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Mal; nucleotides 9062-9082 of the nef1 gene of HIV-Eli; nucleotides 9082-9062 and 9449-9428 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Eli; nucleotides 5073-5099 and 5383-5405 of the vif1 gene of HIV-1 Bru; and nucleotides 5405-5383 and 5675-5653 of a nucleic acid sequence complementary to the vif1 gene of HIV-1 Bru; nucleotides 5068-5094 and 5378-5400 of the vif1 gene of HIV-1 Mal; nucleotides 5400-5378 and 5670-5648 of a nucleic acid sequence complementary to the vif1 gene of HIV-1 Mal; and nucleotides 5037-5063 and 5347-5369 of the vif1 gene of HIV-1 Eli; nucleotides 5369-5347 and 5639-5617 of a nucleic acid sequence complementary to the vif1 gene of HIV-1 Eli; nucleotides 6081-6105 and 6240-6263 of the vpu gene of HIV-1 Bru; nucleotides 6343-6321 of a nucleic acid sequence complementary to the vpu gene of HIV-1 Bru; nucleotides 6076-6100 and 6238-6261 of the vpu gene of HIV-1 Mal; nucleotides 6338-6316 of a nucleic acid sequence complementary to the vpu gene of HIV-1 Mal; nucleotides 6045-6069 and 6207-6230 of the vpu gene of SIV-MAC; and nucleotides 6307-6285 of a nucleic acid sequence complementary to the vpu gene of SIV-MAC.

2. An oligonucleotide primer selected from the group consisting of primers having the following nucleotide sequences from 5' to 3':  
MMy1: TGG CGC CCGAAC AGG GAC TGG CGC CTGAAC AGG GAC MMy2: GGC CAG GGG GAAAGAAAAA GGC CCG GCG GAAAGAAAAA MMy3: TGC CCA TACAAAATG TTT TA TGC CCA CAC TAT ATG TTT TA MMy4: TGC ATG GCT GCT TGA TG TGC ATA GCT GCC TGG TG MMy4B: CTT TGC ATG GCT GCT TGA TG CTC TGC ATA GCT GCT TGC TG MMy4Ba: CAT CAAGCA GCC ATG CAAAG CAC CAG GCA GCT ATG CAG AG MMy28: AGG GCT GTT GGAAAT GTG G AGG GCT GTT GGA AGT GTG G MMy28a: CCA CAT TTC CAG CAT CCC T CCA CAT TTC CAG CAG CCC T CCA CAT TTC CAG CAC CCC T MMy18: GAT AGA TGGAAC AAG CCC CAG MMy19: TCC ATT TCT TGC TCT CCT CTG T MMy29: TAAAGC CAG GAA TGG ATG GCC CAA TAAAGC CAG GAA TGG ATG GAC CAA MMy29a: TTG GGC CAT CCA TTC CTG GCT TTA TTG GTC CAT CCA TTC CTG GCT TTA MMy30: TGG ACT GTC AAT GAC ATA CAGAA TGG ACT GTC AAT GAT ATA CAGAA MMy30a: TTC TGT ATG TCA TTG ACA GTC CA TTC TGT ATG TCA TTG ACT GTC CA MMy31: CAT GGG TAC CAG CAC ACAAAG G MMy31a: CCT TTG TGT GCT GGT ACC CAT G MMy32: TGG AAA GGT GAA GGG GCA GT TGG AAA GGT GAAGGA GCA GT MMy32a: ACT GCC CCT TCA CCT TTC CA ACT GCC CCT TCT CCT TTC CA ACT GCC CCT TCC CCT TTC CA MMy12: AGA GAC TCT TGC GGG CGC GTG MMy13: ATA TAC TTA GAAAAG GAA GAAGG MMy13a: CCT TCT TCC TTT TCTAAG TAT AT MMy14: AGC TGA GAC AGC AGG GAC TTT CCA MMy20: TAT GGA GGA GGAAAAGAG ATG GAT AGT MMy21: TAG CAC TTA TTT CCC TTG CTT T MMy21a: AAA GCA AGG GAAATA AGT GCT A MMy22: CCC TTG TTC ATC ATG CCA GTA T MMy23: ATG TCA GAT CCC AGG GAG A MMy24: CCT GGA GGG GGA GGA GGA GGA MMy5: CCA ATT CCC ATA CAT TAT TGT GCC CC MMy5a: GGG GCA CAA TAATGT ATG GGA ATT GG MMy6: AAT GGC AGT CTA GCA GAA GAA GA MMy7: ATC CTC AOG AGG GGA CCC AGAAAT T MMy7a: AAT TTC TGG GTC CCC TCC TGA GGA T MMy8a: GTG CTT CCT GCT GCT CCC AAG AAC CC MMy8a: GGG TTC TTG GGA GCA GCA GGA AGC AC MMy9: ATG GGT GGC AAG TGG TCAAAAAGT AG ATG GGT GGCAATGG TCAAAAAGT AG MMy9a: CTA CTT TTT GAC CAC TTG CCA CCC AT MMy89: TTC ATT CTT TTC TTG CTG G MMy10: AAAAGAAAAGGG GGG ACT GGA MMy10a: TCC AGT CCC CCC TTT TCT TTT MMy11: AAA GTC CCC AGC

GGAAAG TCC C MMy15: GAT TAT GGAAAA CAG ATG GCA GGT GAT MMy16:  
GCAGAC CAACTA ATT CAT CTG TA MMy16a: TAC AGA TGA ATT AGT TGG TCT  
GC MMy17: CTT AAG CTC CTC TAAAAG CTC TA MMy25: GTA AGT AGT ACA  
TGTAAT GCA ACC T MMy26: AGC AGA AGA CAG TGG CCATGA GAG MMy27: ACT  
ACA GAT CAT CAATAT CCC AA.

3. A method for amplifying nucleic acids of viruses of the HIV-1, HIV-2, and SIV type in a biological sample, said method comprising a) extracting said nucleic acid from said biological sample; b) treating said nucleic acid with a reverse transcriptase if said nucleic acid is RNA; and c) performing an amplification cycle comprising the following steps: denaturing the nucleic acid to be detected to form single-stranded nucleic acids, hybridizing each of said nucleic acid single strands with at least one primer according to any one of claims 1 and 2, by placing said single strands in contact with at least one of said primers, and amplifying said nucleic acid strands by elongation of said primers along the strands to which they are hybridized in the presence of a polymerase, dATP, dGTP, dCTP and dTTP, said cycle being repeated about 30 to about 40 times.

4. The method of claim 3 wherein the step of denaturing the nucleic acid is carried out in the presence of said primer.

5. A method of in vitro diagnosis of infection of a mammal by a virus selected from the group consisting of HIV-1, HIV-2, and SIV, said method comprising detecting nucleic acid of said virus by a) obtaining a biological sample from said mammal, wherein said biological sample comprises nucleic acid; b) extracting nucleic acid of said virus from said biological sample and, if said nucleic acid is RNA, treating said nucleic acid with a reverse transcriptase to produce a double-stranded nucleic acid comprising said nucleic acid and its complementary strand; c) performing an amplification cycle comprising the following steps: denaturing the double-stranded nucleic acid to be detected to form single-stranded nucleic acids, hybridizing each of said nucleic acid single strands with at least one primer according to any one of claims 1 and 2, by placing said single strand in contact with said primer under hybridization conditions, and amplifying said nucleic acid single strands by elongation of said primers along the strands to which they are hybridized in the presence of a polymerase, dATP, dGTP, dCTP and dTTP, said cycle being repeated about 10 to about 60 times; d) detecting the nucleic acid of said virus and e) correlating the presence of the nucleic acid of said virus with infection by said virus.

6. The diagnostic method of claim 5, wherein the hybridization step of the cycle is carried out by placing each of said single-stranded nucleic acids in contact with said primers, wherein said primers hybridize with a nucleotide sequence situated on the first strand of said double-stranded nucleic acid and with a nucleotide sequence situated on the strand complementary to said first strand, said nucleic acid sequences being separated by a region of about 50 to about 10,000 base pairs when said complementary strands are hybridized to form one double-stranded nucleic acid.

7. The method of claim 6, wherein said region is about 100 to about 1100 base pairs.

8. The method according to claim 5, wherein said detecting step (d) comprises hybridizing at least one detectably labelled nucleotide probe to said amplified nucleic acid.

9. The method of claim 5 wherein said virus is HIV-1 or HIV-2, and said primer couple is selected from the group consisting of MMy1-MMy4, MMy2-MMy4, MMy1-MMy3, MMy18-MMy19, MMy4a-MMy28a,

MMy28-MMy29a, MMy29-MMy30a, and MMy31-MMy32a.

10. The method of claim 5 wherein said virus is HIV-1, and said primer couple is selected from the group consisting of MMy5-MMy8, MMy6-MMy8, MMy7-MMy8, MMy5-MMy7a, MMy6-MMy7a, MMy9-MMy11, MMy10-MMy11, MMy9-MMy10a, MMy26-MMy5a, MMy8a-MMy9a, MMy8a-MMy89a, MMy89a-MMy9a, MMy15-MMy17, MMy15-MMy16a, MMy16-MMy17, MMy25-MMy27, and MMy26-MMy27.

11. The method of claim 5, wherein said virus is HIV-2, and said primer, couple is selected from the group consisting of MMy20-MMy22, MMy20-MMy21a, MMy21-MMy22, MMy23-MMy24, MMy12-MMy14, and MMy12-MMy13a.

12. The method of claim 5, wherein said virus comprises a gene selected from the group consisting of gag, vpr, env, nef1, vif1, vif2, vpx, nef2, vpu and pol, and said primer couple is selected from the group consisting of MMy1-MMy4, MMy2-MMy4, MMy1-MMy3, MMy4a-MMy28a for the gag gene; MMy18-MMy19 for the vpr gene; MMy5-MMy8, MMy6-MMy8, MMy7-MMy8, MMy5-MMy7a, MMy6-MMy7a, MMy26-MMy5a, MMy8a-MMy9a, MMy8a-MMy89, MMy89a-MMy9a for the env gene; MMy9-MMy11, MMy9-MMy10a, MMy10-MMy11 for the nef1 gene; MMy15-MMy17, MMy15-MMy16a, MMy16-MMy17 for the vif1 gene; MMy20-MMy22, MMy20-MMy21a, MMy21-MMy22 for the vif2 gene; MMy23-MMy24 for the vpx gene; MMy12-MMy14, MMy12-MMy13a, MMy13-MMy14 for the nef2 gene; MMy25-MMy27, MMy26-MMy27 for the vpu gene; and MMy28-MMy29a, MMy29-MMy30a, MMy30-MMy31a, MMy31-MMy32a for the pol gene.

13. A diagnostic kit for the in vitro diagnosis of infection of a meal by a virus selected from the group consisting of HIV-1, HIV-2, and SIV by detecting the presence of HIV-1, HIV-2 or SIV nucleic acid or a strand of DNA complementary to said nucleic acid, said kit comprising a) at least a first and a second prime according to any one of claims 1 and 2, wherein said first primer is complementary to a region of nucleotides of the nucleic acid of said virus, and said second primer is complementary to a region of nucleotides of the strand of DNA complementary to said nucleic acid of said virus, wherein said regions of nucleotides are separated by about 50 to about 10,000 base pairs when said complementary strands are incorporated into one double-stranded nucleic acid; b) reagents for amplifying said nucleic acid; and c) at least one detectably labelled probe capable of hybridizing with the amplified nucleotide sequence to be detected.

14. An oligonucleotide primer couple for the amplification according to any one of claims 3 and 5, said primer couple selected from the group consisting of MMy4Ba-MMy28a, MMy26-MMy5a, MMy8a-MMy89, MMy89a-MMy9a, MMy25-MMy27, MMy26-MMy27, MMy28-MMy29a, MMy29-MMy30a, MMy30-MMy31a, and MMy31-MMy32a.

L4 ANSWER 17 OF 24 USPATFULL

92:100919 Viral vector coding glycoprotein of HIV-1.

Kieny, Marie-Paule, Strasbourg, France

Rautmann, Guy, Strasbourg, France

Lecocq, Jean-Pierre, Reichstett, France

Hobson, Simon W., Montigny-le-Bretonneux, France

Girard, Marc, Paris, France

\*\*\*Montagnier, Luc\*\*\*, Le Plessis-Robinson, France

Transgene S.A., Institut Pasteur, France (non-U.S. corporation)

US 5169763 921208

APPLICATION: US 91-765413 910924 (7)

PRIORITY: FR 86-5043 860408

FR 86-15106 861029

DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A viral vector comprising at least a portion of the genome of the



HIV virus, a gene coding gp160 glycoprotein of the envelope of the HIV virus, as well as the elements providing for the expression of the glycoprotein in cells, wherein the gp160 is expressed as a non-cleavable protein.

CLM What is claimed is:

1. A viral vector, the genome of which comprises: a functional origin of replication of a poxvirus; a first DNA fragment encoding a non-cleavable gp160, consisting of gp120-gp140, derived from the natural gp160 of an HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequence REKR originally found in the natural gp160; a second DNA fragment encoding a signal peptide, said second DNA fragment being linked to the 5' end of said first DNA fragment; and a promoter for expressing said DNA fragment in mammalian cells.

2. A viral vector according to claim 1, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequences KRR and REKR originally found in the natural gp160.

3. A viral vector according to claim 1, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160.

4. A viral vector according to claim 2, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160, and in that it comprises a 3-amino acid sequence other than KRR in place of the amino acid sequence KRR originally found in the natural gp160.

5. A viral vector according to claim 3, the genome of which comprises a DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being different from the natural gp160 in that the amino acid sequence REKR originally found in the natural gp160 is replaced by the amino acid sequence NEHQ.

6. A viral vector according to claim 4, the genome of which comprises a DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being different from the natural gp160 in that the amino acid sequences KRR and REKR are replaced respectively by the amino acid sequences QNH and NEHQ.

7. A viral vector according to claim 1, the genome of which comprises a first DNA fragment encoding a non-cleavable and soluble gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable and soluble gp160 being different from the natural gp160 in that it does not contain the amino acid sequence REKR originally found in the natural gp160, and in that the transmembrane region originally found in the natural gp160 is deleted.

8. A viral vector according to claim 7, wherein said non-cleavable and soluble gp160 is different from the natural gp160 in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160.

9. A viral vector according to claim 8, wherein said non-cleavable

and soluble gp160 is different from the natural gp160 in that the amino acid sequence REKR originally found in the natural gp160 is replaced by the amino acid sequence NEHQ.

10. A viral vector according to claim 2, the genome of which comprises a first DNA fragment encoding a non-cleavable and soluble gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable and soluble gp160 being different from the natural gp160 in that it does not contain the amino acid sequences KRR and REKR originally found in the natural gp160, and in that the transmembrane region originally found in the natural gp160 is deleted.

11. A viral vector according to claim 10, wherein said non-cleavable and soluble gp160 is different from the natural gp160 in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160, and a 3-amino acid sequence other than KRR in place of the amino acid sequence KRR originally found in the natural gp160.

12. A viral vector according to claim 11, wherein said non-cleavable and soluble gp160 is different from the natural gp160 in that the amino acid sequences KRR and REKR are replaced respectively by the amino acid sequences QNH and NEHQ.

13. A viral vector according to claim 1, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequence REKR originally found in the natural gp160, and in that the transmembrane region originally found in the natural gp160 is replaced by the transmembrane region of the glycoprotein of the rabies virus.

14. A viral vector according to claim 13, wherein said non-cleavable gp160 is characterized in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160.

15. A viral vector according to claim 2, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequences KRR and REKR originally found in the natural gp160, and in that the transmembrane region originally found in the natural gp160 is replaced by the transmembrane region of the glycoprotein of the rabies virus.

16. A viral vector according to claim 15, wherein said non-cleavable gp160 is characterized in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160, and a 3-amino acid sequence other than KRR in place of the amino acid sequence KRR originally found in the natural gp160.

17. A viral vector according to claim 1, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequence REKR originally found in the natural gp160, and in that the amino acid Arg of the transmembrane region originally found in the natural gp160 is replaced by the amino acid Ile.

18. A viral vector according to claim 17, wherein said non-cleavable gp160 is characterized in that it comprises a

4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160.

19. A viral vector according to claim 2, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequences KRR and REKR originally found in the natural gp160, and in that the amino acid Arg of the transmembrane region originally found in the natural gp160 is replaced by the amino acid Ile.

20. A viral vector according to claim 19, wherein said non-cleavable gp160 is characterized in that it comprises a 4-amino acid sequence other than REKR in place of the amino acid sequence REKR originally found in the natural gp160, and a 3-amino acid sequence other than KRR in place of the amino acid sequence KRR originally found in the natural gp160.

21. A viral vector according to claim 1, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequence REKR originally found in the natural gp160, and in that the hydrophobic region proximate to the C-terminal end of the REKR sequence as originally found in the natural gp160 is deleted.

22. A viral vector according to claim 2, the genome of which comprises a first DNA fragment encoding a non-cleavable gp160 derived from the natural gp160 of the HIV-1 virus, said non-cleavable gp160 being characterized in that it does not contain the amino acid sequences REKR and KRR originally found in the natural gp160, and in that the hydrophobic region proximate to the C-terminal end of the REKR sequence as originally found in the natural gp160 is deleted.

23. A viral vector according to claim 1, the genome of which comprises a second DNA fragment encoding a signal peptide which is selected from the group consisting of the signal peptide of the precursor of the gp160 of the HIV-1 virus and the signal peptide of the precursor of the glycoprotein of the rabies virus.

24. A viral vector according to claim 2, the genome of which comprises a second DNA fragment encoding a signal peptide which is selected from the group consisting of the signal peptide of the precursor of the gp160 of the HIV-1 virus and the signal peptide of the precursor of the glycoprotein of the rabies virus.

25. A viral vector according to claim 1, the genome of which comprises a functional origin of replication of a poxvirus.

26. A viral vector according to claim 25, the genome of which comprises a functional origin of replication of a vaccinia virus.

27. A viral vector according to claim 2, the genome of which comprises a functional origin of replication of a poxvirus.

28. A viral vector according to claim 27, the genome of which comprises a functional origin of replication of a vaccinia virus.

29. A viral vector according to claim 1, wherein the DNA encoding envelope protein of HIV-1 is encoded by the EcoRI-KpnI and KpnI-HindIII fragments of plasmid PJ19-13, comprising nucleotides 1258 to 1698 of the DNA encoding envelope protein of HIV-1, and the HindIII-XhoI fragment of plasmid PJ19-6, comprising nucleotides 1698 to 9173 of the DNA encoding envelope protein of

HIV-1.

30. A viral vector according to claim 2, wherein the DNA encoding envelope protein of HIV-1 is encoded by the EcoRI-KpnI and KpnI-HindIII fragments of plasmid PJ19-13, comprising nucleotides 1258 to 1698 of the DNA encoding envelope protein of HIV-1, and the HindIII-XhoI fragment of plasmid PJ19-6, comprising nucleotides 1698 to 9173 of the DNA encoding envelope protein of HIV-1.

31. A culture of mammalian cells, which is infected with a viral vector as claimed in any one of claims 1 to 6 or 13 to 28.

32. A culture of mammalian cells, which is infected with a viral vector as claimed in any one of claims 7 to 12.

33. A process for producing a non-cleavable and soluble gp160 which comprises recovering said non-cleavable gp160 from a culture of mammalian cells as claimed in claim 32.

L5 ANSWER 2 OF 4 USPATFULL

92:86879 Immunoassays for antibody to human immunodeficiency virus using recombinant antigens.

\*\*\*Luciw, Paul A.\*\*\* , Davis, CA, United States  
Dina, Dino, San Francisco, CA, United States  
Chiron Corporation, Emeryville, CA, United States (U.S. corporation)  
US 5156949 921020  
APPLICATION: US 87-138894 871224 (7)  
DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Polynucleotide sequences are provided for the diagnosis of the presence of retroviral infection in a human host associated with lymphadenopathy syndrome and/or acquired immune deficiency syndrome, for expression of polypeptides and use of the polypeptides to prepare antibodies, where both the polypeptides and antibodies may be employed as diagnostic reagents or in therapy, e.g., vaccines and passive immunization. The sequences provide detection of the viral infectious agents associated with the indicated syndromes and can be used for expression of antigenic polypeptides.

L8 ANSWER 5 OF 5 MEDLINE

85086249 Document Number: 85086249. Molecular cloning of lymphadenopathy-associated virus. \*\*\*Alizon M\*\*\* ; Sonigo P; Barre-Sinoussi F; Chermann J C; Tiollais P; Montagnier L; Wain-Hobson S. NATURE, (1984 Dec 20-1985 Jan 2) 312 (5996) 757-60. Journal code: NSC. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Lymphadenopathy-associated virus ( \*\*\*LAV\*\*\* ) is a human retrovirus first isolated from a homosexual patient with lymphadenopathy syndrome, frequently a prodrome or a benign form of acquired immune deficiency syndrome (AIDS). Other \*\*\*LAV\*\*\* isolates have subsequently been recovered from patients with AIDS or pre-AIDS and all available data are consistent with the virus being the causative agent of AIDS. The virus is propagated on activated T lymphocytes and has a tropism for the T-cell subset OKT4 (ref. 6), in which it induces a cytopathic effect. The major core protein of \*\*\*LAV\*\*\* is antigenically unrelated to other known retroviral antigens. \*\*\*LAV\*\*\* -like viruses have more recently been independently isolated from patients with AIDS and pre-AIDS. These viruses, called human T-cell leukaemia/lymphoma virus type III (HTLV-III) and AIDS-associated retrovirus (ARV), seem to have many characteristics in common with \*\*\*LAV\*\*\* and probably represent independent isolates of the \*\*\*LAV\*\*\* prototype. We have sought to characterize \*\*\*LAV\*\*\* by the molecular cloning of its genome. A cloned \*\*\*LAV\*\*\* complementary DNA was used to screen a library of recombinant phages constructed from the genomic DNA of

\*\*\*LAV\*\*\* -infected T lymphocytes. Two families of clones were characterized which differ in a restriction site. The viral genome is longer than any other human retroviral genome (9.1-9.2

L8 ANSWER 4 OF 5 MEDLINE

85099333 Document Number: 85099333. Nucleotide sequence of the AIDS virus, \*\*\*LAV\*\*\*. Wain-Hobson S; Sonigo P; Danos O; Cole S; \*\*\*Alizon M\*\*\*. CELL, (1985 Jan) 40 (1) 9-17. Journal code: CQ4. ISSN: 0092-8674. Pub. country: United States. Language: English.  
AB The complete 9193-nucleotide sequence of the probable causative agent of AIDS, lymphadenopathy-associated virus (\*\*\*LAV\*\*\*), has been determined. The deduced genetic structure is unique: it shows, in addition to the retroviral gag, pol, and env genes, two novel open reading frames we call Q and F. Remarkably, Q is located between pol and env and F is half-encoded by the U3 element of the LTR. These data place \*\*\*LAV\*\*\* apart from the previously characterized family of human T cell leukemia/lymphoma viruses.

L8 ANSWER 2 OF 5 MEDLINE

86294252 Document Number: 86294252. Lymphadenopathy/AIDS virus: genetic organization and relationship to animal lentiviruses. \*\*\*Alizon M\*\*\*; Montagnier L. ANTICANCER RESEARCH, (1986 May-Jun) 6 (3 Pt B) 403-11. Journal code: 59L. ISSN: 0250-7005. Pub. country: Greece. Language: English.  
AB This article presents data obtained by our group in the molecular characterization of the probable agent of the acquired immune deficiency syndrome (AIDS), the lymphadenopathy/AIDS virus (\*\*\*LAV\*\*\*). Molecular cloning and complete nucleotide sequencing of \*\*\*LAV\*\*\* allows a detailed comparison with other AIDS virus isolates, as well as other human and animal retroviruses. We have now molecular evidence that the AIDS virus is closely related to visna virus, prototype of the lentiviruses, whereas the other human retroviruses, i.e., human T-cell leukemia viruses type I and II (HTLV-I and II), are quite remote in the evolution.

L9 ANSWER 25 OF 30 MEDLINE

86245056 Document Number: 86245056. Genetic variability of the AIDS virus: nucleotide sequence analysis of two isolates from African patients. \*\*\*Alizon M\*\*\*; Wain-Hobson S; Montagnier L; Sonigo P. CELL, (1986 Jul 4) 46 (1) 63-74. Journal code: CQ4. ISSN: 0092-8674. Pub. country: United States. Language: English.  
AB To define further the genetic variability of the human AIDS retrovirus, we have cloned and sequenced the complete genomes of two isolates obtained from Zairian patients. Their genetic organization is identical with that of isolates from Europe and North America, confirming a common evolutionary origin. However, the comparison of homologous proteins from these different isolates reveals a much greater extent of genetic polymorphism than previously observed. It is nevertheless possible to define conserved domains in the viral proteins, especially in the envelope, that could be of interest for the understanding of the molecular mechanisms of viral pathogenicity and for the development of diagnostic and therapeutic reagents.

L15 ANSWER 4 OF 8 MEDLINE

85270417 Document Number: 85270417. Genomic diversity of the acquired immune deficiency syndrome virus HTLV-III: different viruses exhibit greatest divergence in their envelope genes. \*\*\*Hahn B H\*\*\*; Gonda M A; Shaw G M; Popovic M; Hoxie J A; Gallo R C; Wong-Staal F. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, \*\*\* (1985 Jul) \*\*\* 82 (14) 4813-7. Journal code: PV3. ISSN: 0027-8424. Pub. country: United States. Language: English.  
AB Converging lines of research have linked human T-cell lymphotropic virus type III (HTLV-III) to the pathogenesis of the acquired immune deficiency syndrome. A characteristic feature of this virus is its genomic heterogeneity, which occurs to varying degrees in different viral isolates. To define further the nature and extent of these genomic changes, we compared the molecularly cloned genomes of two

variant HTLV-III isolates by extensive restriction enzyme mapping and heteroduplex thermal melt analysis. Both viral isolates were found to be highly related to each other throughout their entire genomic complement, yet they differed markedly in their restriction enzyme maps. Electron microscopic heteroduplex analysis revealed several distinct regions of divergence located almost exclusively in the part of the genome that encodes the viral envelope gene. In vitro culture of one of these viruses over a period of 3 months did not result in any genomic changes as determined by restriction analysis of viral DNA. These results, as well as the recently published nucleotide sequences of other HTLV-III isolates, indicate that the most substantial variation among HTLV-III isolates is located in the envelope. These findings raise the possibility that viral isolates from different individuals could have important biological differences in their envelope antigens, a consideration relevant to ongoing attempts to develop a vaccine against HTLV-III.

L15 ANSWER 2 OF 8 MEDLINE

85272575 Document Number: 85272575. Genomic diversity of human T-lymphotropic virus type III (HTLV-III). Wong-Staal F; Shaw G M; \*\*\*Hahn B H\*\*\* ; Salahuddin S Z; Popovic M; Markham P; Redfield R; Gallo R C. SCIENCE, \*\*\* (1985 Aug 23) \*\*\* 229 (4715) 759-62. Journal code: UJ7. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB The DNA genomes of human T-lymphotropic virus type III (HTLV-III) isolated from 18 individuals with AIDS or who were at risk for AIDS were evaluated for evidence of variation. Although all of the 18 viral DNA's hybridized throughout their entire genomes to a full-length cloned probe of the original HTLV-III isolate, each of the 18 isolates showed a different restriction enzyme pattern. The number of restriction site differences between isolates ranged from only 1 site in 23 to at least 16 sites in 31. No particular viral genotype was associated with a particular disease state and 2 of the 18 patients had evidence of concurrent infection by more than one viral genotype. Propagation of three different viral isolates in vitro for up to 9 months did not lead to detectable changes in their restriction patterns. These findings indicate that different isolates of HTLV-III comprise a spectrum of highly related but distinguishable viruses and have important implications regarding the pathogenicity of HTLV-III and attempts to develop effective diagnostic, therapeutic, and preventive measures for this virus.

L16 ANSWER 3 OF 3 MEDLINE

86218077 Document Number: 86218077. Identification and characterization of conserved and variable regions in the envelope gene of HTLV-III/LAV, the retrovirus of AIDS. Starcich B R; \*\*\*Hahn B H\*\*\* ; Shaw G M; McNeely P D; Modrow S; Wolf H; Parks E S; Parks W P; Josephs S F; Gallo R C; et al. CELL, \*\*\* (1986 Jun) \*\*\* 6) \*\*\* 45 (5) 637-48. Journal code: CQ4. ISSN: 0092-8674. Pub. country: United States. Language: English.

AB To determine the extent and nature of genetic variation present in independent isolates of HTLV-III/LAV, the nucleotide sequences of the entire envelope gene and parts of gag and pol were determined for two AIDS viruses. The results indicated that variation throughout the viral genome is extensive and that the envelope gene in particular is most highly variable. Within the envelope, changes were most prevalent within the extracellular region where clustered nucleotide substitutions and deletions/insertions were evident. Based on predicted secondary protein structure and hydrophilicity, these hypervariable regions represent potential antigenic sites. In contrast to the hypervariable regions, other sequences in the extracellular envelope and the overall envelope structure (including 18 of 18 cysteine residues), as well as most of the transmembrane region, were highly conserved.

L16 ANSWER 2 OF 3 MEDLINE

86235450 Document Number: 86235450. Genetic variation in HTLV-III/LAV

- over time in patients with AIDS or at risk for AIDS. \*\*\*Hahn B\*\*\*  
\*\*\* H\*\*\* ; Shaw G M; Taylor M E; Redfield R R; Markham P D; Salahuddin  
S Z; Wong-Staal F; Gallo R C; Parks E S; Parks W P. SCIENCE,  
\*\*\* (1986 Jun 20) \*\*\* 232 (4757) 1548-53. Journal code: UJ7. ISSN:  
0036-8075. Pub. country: United States. Language: English.
- AB In a study of genetic variation in the AIDS virus, HTLV-III/LAV,  
sequential virus isolates from persistently infected individuals  
were examined by Southern blot genomic analysis, molecular cloning,  
and nucleotide sequencing. Four to six virus isolates were obtained  
from each of three individuals over a 1-year or 2-year period.  
Changes were detected throughout the viral genomes and consisted of  
isolated and clustered nucleotide point mutations as well as short  
deletions or insertions. Results from genomic restriction mapping  
and nucleotide sequence comparisons indicated that viruses isolated  
sequentially had evolved in parallel from a common progenitor virus.  
The rate of evolution of HTLV-III/LAV was estimated to be at least  
10(-3) nucleotide substitutions per site per year for the env gene  
and 10(-4) for the gag gene, values a millionfold greater than for  
most DNA genomes. Despite this relatively rapid rate of sequence  
divergence, virus isolates from any one patient were all much more  
related to each other than to viruses from other individuals. In  
view of the substantial heterogeneity among most independent  
HTLV-III/LAV isolates, the repeated isolation from a given  
individual of only highly related viruses raises the possibility  
that some type of interference mechanism may prevent simultaneous  
infection by more than one major genotypic form of the virus.
- L17 ANSWER 103 OF 125 MEDLINE  
86098667 Document Number: 86098667. Transactivation induced by human  
T-lymphotropic virus type III (HTLV III) maps to a viral sequence  
encoding 58 amino acids and lacks tissue specificity. Seigel L J;  
\*\*\*Ratner L\*\*\* ; Josephs S F; Derse D; Feinberg M B; Reyes G R;  
O'Brien S J; Wong-Staal F. VIROLOGY, (1986 Jan 15) 148 (1) 226-31.  
Journal code: XEA. ISSN: 0042-6822. Pub. country: United States.  
Language: English.
- L17 ANSWER 107 OF 125 MEDLINE  
85268015 Document Number: 85268015. A molecular clone of HTLV-III with  
biological activity. Fisher A G; Collalti E; \*\*\*Ratner L\*\*\* ;  
Gallo R C; Wong-Staal F. NATURE, (1985 Jul 18-24) 316 (6025) 262-5.  
Journal code: NSC. ISSN: 0028-0836. Pub. country: ENGLAND: United  
Kingdom. Language: English.
- L17 ANSWER 108 OF 125 MEDLINE  
85254466 Document Number: 85254466. Molecular biology of human  
T-lymphotropic retroviruses. Wong-Staal F; \*\*\*Ratner L\*\*\* ; Shaw  
G; Hahn B; Harper M; Franchini G; Gallo R. CANCER RESEARCH, (1985  
Sep) 45 (9 Suppl) 4539s-4544s. Ref: 52. Journal code: CNF. ISSN:  
0008-5472. Pub. country: United States. Language: English.
- L17 ANSWER 92 OF 125 MEDLINE  
87299196 Document Number: 87299196. Complete nucleotide sequences of  
functional clones of the AIDS virus. \*\*\*Ratner L\*\*\* ; Fisher A;  
Jagodzinski L L; Mitsuya H; Liou R S; Gallo R C; Wong-Staal F. AIDS  
RESEARCH AND HUMAN RETROVIRUSES, (1987 Spring) 3 (1) 57-69. Journal  
code: ART. ISSN: 0889-2229. Pub. country: United States. Language:  
English.